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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

NATARAJAN, MEERA

ART UNIT

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1643

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/593,859	Applicant(s) LOMBARDO ET AL.	
	Examiner MEERA NATARAJAN	Art Unit 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 May 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 41-62 is/are pending in the application.
- 4a) Of the above claim(s) 46-62 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 41-45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>05/15/2007 and 06/23/2008</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, Claims 41-45 in the reply filed on 05/30/2008 is acknowledged.
2. Claims 46-62 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 05/30/2008.
3. Claims 41-45 will be examined on the merits.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
5. Claim 41 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
6. Claim 41 recites "or derivative thereof". The metes and bounds of the phrase "derivative" are unclear because the exact meaning of the phrase is not clear. The term "derivative" is not one which has a universally accepted meaning in the art nor is it one which has been adequately defined in the specification. The primary deficiency in the use of this phrase is the absence of an ascertainable meaning for said phrase. Since it is unclear how the antibodies are to be derivatized to yield the class of derivatives referred to in the claims, there is no way for a person of skill in the art to ascribe a

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discrete and identifiable class of compounds to said phrase. Further, it is not clear whether the “derivative” of the antibody is formed by attachment of a detectable marker, therapeutic molecule, some other molecule or altering the amino acid sequence, for examples. In addition, since the term “derivative” does not appear to be clearly defined in the specification, and the term can encompass proteins with amino acid substitutions, insertions, or deletions, antibody fragments, chemically derivatized molecules, or even antibody mimetics. In absence of a single defined art recognized meaning for the phrase and lacking a definition of the term in the specification, one of skill in the art could not determine the metes and bounds of the claims.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 41-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. *The following grounds of rejection pertain to an antibody without antigen specificity.*

9. Antibodies are glycoproteins that possess the ability to react in vitro and in vivo specifically and selectively with the antigenic determinants or epitopes eliciting their production or with an antigenic determinant closely related to the homologous antigen.

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Antibodies are immunoglobulins that are formed in response to immunogens or that are screened for specificity to an antigen/immunogen.

10. It has been well established in the art that the antigen binding specificity is critical to how the skilled artisan would employ antibodies in various modalities (e.g., affinity purification, detection or diagnostic assays, bioassays, treatment), including those consistent with the instant disclosure (see specification, including the Summary of the Invention).

11. However, the instant claims do not recite an antigen specificity for the 16D10 antibody. The specification provides insufficient direction or guidance regarding how to use antibodies comprising the claimed sequences *in the absence of an antigen specificity* for BSDL or FAPP and yet retain substantially the same binding specificity of the 16D10 antibody and antigen-binding fragments thereof, which are enabling consistent with the disclosed utilities of the instant disclosure (see Detailed Description / claims, etc.)

12. Given the well known polymorphism of antibodies, it would have been undue experimentation to make and use the vast repertoire of antibodies encompassed by the claimed invention in the absence of binding specificity for BSDL or FAPP to enable the scope of the claimed antibodies encompassed by the claimed invention.

13. Without sufficient guidance and given the well known complexity and unpredictability of using antibodies with no particular antigen specificity as well the well known polymorphism of antibodies; it would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue to

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make and use the vast repertoire of antibodies broadly encompassed by the claimed invention in order to make and use the 16D10 antibody consistent with the instant disclosure.

14. Applicant is invited to amend the claims to recite the appropriate antigen specificity to obviate this rejection.

15. Claims 41-45 are rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure without complete evidence either that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological materials.

16. The specification lacks deposit information for the deposit of 16D10. It is not clear that the antibody recited in the claims is known and publicly available or can be reproducibly isolated from nature without undue experimentation. Because one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed in the absence of the availability of the claimed antibodies, a suitable deposit of the antibodies, evidence of public availability of the claimed antibodies or evidence of the reproducibility without undue experimentation of the claimed antibodies, is required.

17. If the deposit is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit of 16D10 has been accepted by an

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International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

18. If the deposit is not made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

19. Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit

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and maintenance of each deposit.

20. If a deposit is made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

Claim Rejections - 35 USC § 102

21. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

22. Claim 41 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Holmes et al. (Hybridoma, Vol. 19, No. 6, p.503, 2000).

23. The Claims are drawn to a monoclonal antibody selected from the monoclonal antibody 16D10, an antigen binding fragment or derivative thereof, or an antibody which essentially binds to the same epitope as monoclonal antibody 16D10, wherein the antibody is of the IgG type.

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24. Holmes et al. teach a monoclonal 16D10 antibody of IgG type and therefore reads on the claimed 16D10 antibody, derivative thereof, or an antibody which essentially binds to the same epitope as monoclonal antibody 16D10. See 112 1st and 2nd paragraph rejections above for not reciting the specific antigen and the broad scope of "derivative".

25. Claims 41 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Takeda et al. (J. Cancer Res. Clin. Oncol., Volume 118(5), pp.377-385, May 1992).

26. The Claims are drawn to a monoclonal antibody selected from the monoclonal antibody 16D10, an antigen binding fragment or derivative thereof, or an antibody which essentially binds to the same epitope as monoclonal antibody 16D10, wherein the antibody is of the IgG type.

27. Takeda et al. teach the monoclonal antibody J28 of IgG1 subclass which binds to human fetoacinar pancreatic protein (FAPP). The specification discloses "the antibody essentially binds to the same epitope as the monoclonal antibody 16D10 or J28" and binds to FAPP or BSDL. Therefore, Takeda et al. teach the limitations of claims 41 and 43.

Claim Rejections - 35 USC § 103

28. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

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invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

29. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148

USPQ 459 (1966), that are applied for establishing a background for determining

obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

30. Claims 41-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holmes et al. in view of Queen et al. (Patent #6,180,370) and Thirion et al. (European J. of Cancer Prevention, Vol. 5(6), pp.507-511, 1996).

31. The teachings of Holmes et al. is presented in the 102(b) rejection set forth above. Holmes et al. does not teach single-chain, humanized, chimeric antibodies and a kit comprising said antibodies. These deficiencies are made up for in Queen et al. and Thirion et al.

32. Queen et al. teach a method for preparing chimeric and humanized immunoglobulins for novel therapeutic agents (see Examples 6-9) and kits (see Column 25, last paragraph) comprising said antibodies. Queen et al. disclose the potential advantages of humanized antibodies over mouse antibodies for use in human therapy (see Column 16).

33. Thirion et al. teach the advantages of single-chain antibody fragments for solid tumor cancer therapy. Thirion et al. disclose single chain antibodies clear more rapidly from the blood and penetrate faster and deeper into tissues than whole antibodies.

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Furthermore, the lack of constant regions ensures that they are not retained in tissues such as the liver and kidney. This reduces possible toxic side-effects (see Abstract).

34. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed inventions was made to produce a single-chain, humanized, or chimeric version of the 16D10 antibody taught my Holmes et al. and a kit comprising said antibodies. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success based on the teachings of Holmes et al. that 16D10 targets a human antigen and the teachings of Queen et al. and Thirion et al. that chimeric, humanized and single chain antibodies have potential advantages over mouse whole antibodies for use in human therapy.

35. Claims 41-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takeda et al. in view of Queen et al. (Patent #6,180,370) and Thirion et al. (European J. of Cancer Prevention, Vol. 5(6), pp.507-511, 1996).

36. The teachings of Takeda et al. is presented in the 102(b) rejection set forth above. Takeda et al. does not teach single-chain, humanized, chimeric antibodies and a kit comprising said antibodies. These deficiencies are made up for in Queen et al. and Thirion et al.

37. Queen et al. teach a method for preparing chimeric and humanized immunoglobulins for novel therapeutic agents (see Examples 6-9) and kits (see Column 25, last paragraph) comprising said antibodies. Queen et al. disclose the potential

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advantages of humanized antibodies over mouse antibodies for use in human therapy (see Column 16).

38. Thirion et al. teach the advantages of single-chain antibody fragments for solid tumor cancer therapy. Thirion et al. disclose single chain antibodies clear more rapidly from the blood and penetrate faster and deeper into tissues than whole antibodies.

Furthermore, the lack of constant regions ensures that they are not retained in tissues such as the liver and kidney. This reduces possible toxic side-effects (see Abstract).

39. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed inventions was made to produce a single-chain, humanized, or chimeric version of the monoclonal J28 antibody taught by Takeda et al. and a kit comprising said antibodies. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success based on the teachings of Takeda et al. that J28 targets human FAPP antigen and the teachings of Queen et al. and Thirion et al. that chimeric, humanized and single chain antibodies have potential advantages over mouse whole antibodies for use in human therapy.

Conclusion

40. Claims 41-45 are rejected.

41. No Claim is allowed.

42. Any inquiry concerning this communication or earlier communications from the examiner should be directed to MEERA NATARAJAN whose telephone number is

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(571)270-3058. The examiner can normally be reached on Monday-Thursday, 9:30AM-7:00PM, ALT. Friday. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MN

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643